The Honorable Cathy Seibel United States Courthouse 300 Quarropas St. White Plains, NY 10601

August 31, 2018

Dear Judge Seibel:

I was requested by the attorney Alexei Schacht to give my expert opinion regarding gambling disorders and how they may relate to Mr. Michael Scronic and United States v. Michael Scronic, 18CR43 (CS). I was also asked to describe the current state of our knowledge about gambling disorder (previously termed pathological gambling).

I. Qualifications and Experience

I graduated summa cum laude from Yale College in 1987 with B.S./M.S. degrees in Molecular Biophysics and Biochemistry. I then entered the Medical Scientist Training Program at the Yale School of Medicine. In the program, I received my Ph.D. in Cell Biology in 1993 and M.D. in 1994, with honors including awards for best thesis. I entered the Yale Residency Program in Psychiatry and received multiple awards for outstanding clinical and research work during my residency. I was chief resident of the Clinical Neuroscience Research Unit and President of the Yale Psychiatry Residents Association. Following residency, I completed training in the Addiction Psychiatry fellowship program at Yale during which time I received additional awards including an outstanding research award from the American Psychiatric Association.

I am now a Professor of Psychiatry at the Yale University School of Medicine. I hold secondary appointments in the Department of Neuroscience and within the Yale Child Study Center. I am also a Senior Scientist with the Connecticut Council on Problem

1

Gambling. I have over 20 years of experience studying addictive disorders relating to substance use and gambling. I am the Founding Director of Yale's Problem Gambling Clinic, the Women and Addictions Core of Women's Health Research at Yale, the Yale Research Program on Impulsivity and Impulse Control Disorders, and the Yale Center of Excellence in Gambling Research at the Yale School of Medicine. In addition, I serve as the Chair of the Pharmacy and Therapeutics Committee for the Connecticut Mental Health Center and Medical Director and Consulting Psychiatrist for the State of Connecticut's Problem Gambling Treatment Program in the New Haven area.

I have been certified by the American Board of Psychiatry and Neurology in Psychiatry since 2000. Additionally, I was certified by the American Board of Psychiatry and Neurology in Addiction Psychiatry in 2002. I have been or am an active member of the American College of Neuropsychopharmacology, American Psychiatric Association (Member and Fellow), American Academy for Advancement in Science, Society of Biological Psychiatry, and the Society for Neuroscience, among others. I am a founding member of the International Society for Research on Impulsivity and Impulse Control Disorders, was the President of the Society for two years, and am currently one of four atlarge members/advisors. I was on the Advisory Board to the National Council on Problem Gambling for 6 years. I was recently awarded a lifetime achievement award for gambling research by the National Council on Problem Gambling.

Over the past twenty years, I have seen hundreds of individuals with gambling disorder and other addictive disorders. I have seen hundreds of individuals with drug-use problems in my research and non-research clinical capacities.

Throughout my academic career, I have given numerous lectures and courses on gambling disorder and other addictions. I currently serve on the editorial boards of 15 academic journals related to psychiatry, addiction, and gambling, including *The Journal of Gambling Studies*, *The American Journal on Addictions, The Journal of Adolescent Health, The Journal of Addiction Medicine, The Journal of Behavioral Addictions, PloS One,* and *Frontiers in Psychiatry*. I am editor-in-chief of *Current Addiction Reports*. In addition, I have authored or co-authored over 500 articles, case reports, and book chapters concerning gambling behaviors, gambling disorder and other topics.

II. What is Gambling and How Many People Gamble?

Gambling has been defined as placing something of value at risk (usually money) in the hopes of gaining something of greater value (Potenza, Kosten et al. 2001). Many forms of gambling exist, and popular forms in current societies include lotteries, card gambling, sports gambling and electronic gambling machines (EGMs - including slot machines). In the United States, multiple studies have found that the majority of adults gamble. For example, a relatively recent population-based study conducted in the United States estimated lifetime gambling among 78.4% of respondents (Kessler, Hwang et al. 2008).

III. What are Gambling Problems and How Many Have Gambling Problems?

Although most adults gamble, few develop gambling problems. In order to consider who has a gambling problem, how a gambling problem is defined warrants consideration. Historically, many terms have been applied to excessive forms of gambling. In this letter, I primarily use the term "gambling disorder" given that it is the term currently applied in the 5th edition of the Diagnostic and Statistical Manual (DSM-5) of the

American Psychiatric Association (Association 2013), although most studies have been conducted focused on this construct of "pathological gambling."

The DSM represents a repository of clinical diagnoses with explicit diagnostic criteria to assist psychiatrists and others in diagnosing individuals with specific mental health disorders. A category for excessive gambling, termed gambling disorder, was first introduced into the DSM as "pathological gambling" in its third edition in 1980. The term "compulsive gambling" was avoided because there was some apparent concern that "compulsive gambling" might link the disorder to obsessive-compulsive disorder, and the expert consensus group wished to avoid such possible confusion.

Since the introduction of criteria for pathological gambling in DSM-III in 1980, the threshold for determining a "case" of gambling disorder has been debated and evolved through several formulations. The diagnostic criteria in DSM-IV and DSM-IV-TR (Association 2000) included 10 inclusionary criteria and 1 exclusionary criterion – the gambling behavior is not better accounted for by a manic episode. The central element is "persistent and recurrent maladaptive gambling behavior" as evidenced by 5 or more of the 10 inclusionary criteria. The inclusionary criteria from DSM-IV-TR are as follows:

- 1) is preoccupied with gambling (e.g., preoccupied with reliving past gambling experiences, handicapping, or planning the next venture, or thinking of ways to get money with which to gamble)
- needs to gamble with increasing amounts of money in order to achieve the desired excitement
- 3) has repeated unsuccessful attempts to control, cut back, or stop gambling
- 4) is restless or irritable when attempting to cut down or stop gambling

- gambles as a way of escaping from problems or of relieving a dysphoric mood (e.g., feelings of helplessness, guilt, anxiety, depression)
- 6) after losing money, often returns another day to get even ("chasing" one's losses)
- 7) lies to family members, therapist, or others to conceal the extent of involvement with gambling
- 8) has committed illegal acts such as forgery, fraud, theft or embezzlement to finance gambling
- has jeopardized or lost a significant relationship, job, or educational or career opportunity because of gambling
- 10) relies on others to provide money to relieve a desperate financial situation caused by gambling (Association 2000)

The current edition of the DSM (DSM-5 (Association 2013)) involved a renaming of pathological gambling (the gambling-related diagnostic entity in DSM-III and DSM-IV) to "gambling disorder." Additionally, the disorder was reclassified in the category of "Substance-related and Addictive Disorders," with the change based on similarities between substance-use and gambling disorders (Association 2013). Additional changes were made including the elimination of the "illegal acts" criterion, the changing of the diagnostic thresholding from five of ten inclusionary criteria to four of nine, and the specification of a timeframe for the occurrence of the criteria (within a twelve-month period) (Association 2013). These changes were based on the findings of systematic reviews of the literature conducted in expert research work groups (Petry 2006, Potenza 2006, Potenza, Koran et al. 2009), empirical data (Petry, Blanco et al. 2013) and the work

of expert committees involved in the DSM-5 process (Petry, Blanco et al. 2014). These changes were also believed not to impact prevalence estimates.

Psychiatric diagnoses per diagnostic criteria such as defined in the DSM-IV and DSM-5 are considered the "gold standard" for defining cases of a specific disorder and are critical to understanding the prevalence of the disorder. However, prevalence estimates of gambling disorder have been complicated for multiple reasons, including changing diagnostic criteria. Screening instruments based on the DSM criteria have generated estimates for pathological gambling in community samples in the United States. For example, the Gambling Impact and Behavior Study found in a sample of 2,417 individuals surveyed via telephone past-year and lifetime prevalence estimates for pathological gambling of 0.1% and 0.8%, respectively (Hoffmann 1999).

More recently, a large community survey was performed in the United States by the National Institute on Alcohol Abuse and Alcoholism. This survey, the National Epidemiological Survey of Alcohol and Related Conditions (NESARC), included over 43,000 participants. Past-year and lifetime prevalence estimates for pathological gambling were 0.2% and 0.4%, respectively (Petry, Stinson et al. 2005).

The factors that contribute to the development of gambling disorder are not well understood. At times concerns have been raised that with increasing availability of and social acceptedness of gambling, that increases in gambling problems would be observed. However, the preponderance of data does not support this concern. Although the findings are complicated in some cases by the use of different instruments across different studies in some cases, the use of similar instruments in some studies (Welte, Barnes et al. 2015); see also (Abbott, Romild et al. 2014) below) suggest that there are not increases in problem

gambling over time despite the increased availability of some forms of gambling, including casinos (although see (Welte, Tidwell et al. 2016)).

IV. Biospsychosocial Formulations: A Biological Component

Much research has been performed recently in the area of gambling disorder (Institute for Research on Pathological Gambling and Related Disorders 2006, Potenza 2006). As in other areas of psychiatry, there has been a substantial increase in neurobiological research in gambling studies, although the number of neurobiological studies investigating gambling disorder has historically been relatively small (Eber and Shaffer 2000). Thus, much remains to be learned regarding the mechanisms underlying gambling disorder. Given the research over the past two decades, our understanding of the biology underlying gambling disorder has grown significantly.

Multiple neurotransmitter systems have been suggested to contribute to gambling disorder (Potenza 2008, Bullock and Potenza 2012, Leeman and Potenza 2012, Yip and Potenza 2014). Among the most widely implicated neurotransmitters are serotonin, dopamine, norepinephrine, and opioids. It has been hypothesized that these systems are particularly important for particular aspects of gambling disorder: serotonin underlying impaired impulse control, dopamine differential reward and reinforcement, norepinephrine arousal and excitement, and opioids pleasure and urges (Potenza 2008). This explanation is likely overly simplistic. For example, noradrenergic systems have been implicated in cognitive processes, particularly in attention and regulating impulsivity (Arnsten 2001, Arnsten and Li 2005). It is possible that these different neurotransmitters contribute to multiple behaviors and aspects thereof, consistent with the complexities of each of these systems. Additionally, more recent data support a role for the involvement of glutamate,

an abundant excitatory neurotransmitter, in gambling disorder (Grant, Kim et al. 2007, Grant, Odlaug et al. 2010, Leeman and Potenza 2012, Yip and Potenza 2014). Like other psychiatric disorders, gambling disorder is likely heterogeneous with different constellations of specific biological, social and environmental factors contributing to the disorder in individual cases.

The potential relevance of five major neurotransmitter systems with respect to gambling disorder is discussed below, as are genetic and neural contributions.

Norepinephrine Systems

Reports from the 1980's published in the leading journal Archives of General Psychiatry suggested an important role for noradrenergic systems in gambling disorder (Roy, Adinoff et al. 1988, Roy, de Jong et al. 1989). Norepinephrine systems have been hypothesized to mediate aspects of attention, arousal and sensation-seeking in gambling disorder (Potenza 2008). Studies measuring norepinephrine and its metabolites 3methoxy-4-hydroxyphenyl glycol (MHPG) and vanillylmandelic acid (VMA) have found in individuals with gambling disorder higher levels of MHPG in CSF and higher levels of norepinephrine in urine as compared to levels in individuals without gambling disorder (Roy, Adinoff et al. 1988). Positive associations were also found between multiple measures of noradrenergic function and levels of extraversion as assessed by the Eysenck Personality Questionnaire (Roy, de Jong et al. 1989). Furthermore, the desire to start or continue gambling correlated positively with norepinephrine levels among all gamblers (Meyer, Schwertfeger et al. 2004). A pilot investigation with the alpha-2 adrenoreceptor antagonist yohimbine suggests a possible role for adrenergic involvement as related to stress responses in gambling disorder (Elman, Beccera et al. 2012). Although preliminary in that these studies typically included small, predominantly male samples, the data suggest a role for norepinephrine in the maintenance of gambling and the pathophysiology of gambling disorder.

Serotonin Systems

An important role for serotonin in pathological gambling and other impulse control disorders was described in the 1990's (DeCaria 1993, Hollander 1995, Hollander 1998). Multiple lines of evidence support a role for serotonin in gambling disorder and other disorders characterized by impaired impulse control. For several decades, it has been observed that various groups of individuals demonstrating impaired impulse control (e.g., individuals with alcoholism, pyromania, and impulsive aggression) showed low levels of the serotonin metabolite 5-hydroxy-indole-acetic acid (5-HIAA) in their cerebrospinal fluid (CSF) (Potenza and Hollander 2002). More recently, low levels of 5HIAA have been reported in the CSF samples of men with gambling disorder (Nordin and Eklundh 1999). Responses to serotonergic drugs have also been found to differ between groups characterized by impaired impulse control and those who are not. In addition to the subjective measures, individuals with gambling disorder showed greater prolactin release associated with m-CPP administration, with gambling severity correlating with prolactin measures (DeCaria, Begaz et al. 1998).

The ventromedial prefrontal cortex (vmPFC) is a serotonergically innervated region that has been implicated in gambling disorder and other disorders characterized by impaired impulse control. Serotonin function within the vmPFC has been specifically implicated in impulse control disorders. More recently, diminished activation of the vmPFC has been observed in individuals with gambling disorder during gambling urges

(Potenza, Steinberg et al. 2003), cognitive control (involving attention and inhibition of pre-potent responses) (Potenza, Leung et al. 2003), and simulated gambling (Reuter, Raedler et al. 2005). In this second study, the brain region most distinguishing individuals with pathological gambling from control subjects was virtually the same as that distinguishing bipolar subjects from control subjects during performance of the same task (Blumberg, Leung et al. 2003), further suggesting that function of this brain region is important in influencing impaired impulse control across diagnostic boundaries and providing a possible biological explanation for why drugs that are used in the treatment of bipolar disorder may help to reduce both problem-gambling severity and mania in people with gambling disorder and bipolar spectrum disorders (Hollander, Pallanti et al. 2005). *Opioid Systems*

The opioid system has been hypothesized to underlie pleasures and urges in gambling disorder (Potenza 2008). Arguably the strongest support for the importance of mu-opioid systems in gambling disorder comes from clinical trials of mu-opioid receptor antagonists (Kim, Grant et al. 2001, Grant, Potenza et al. 2006, Grant, Kim et al. 2008, Grant, Kim et al. 2008, Grant, Collaug et al. 2010). Four placebo-controlled trials have found the mu-opioid receptor antagonists naltrexone and nalmefene to be superior to placebo in the reduction of gambling thoughts and behaviors (Kim, Grant et al. 2001, Grant, Potenza et al. 2006, Grant, Kim et al. 2008, Grant, Odlaug et al. 2010). Recent research has also suggested blunted stimulant-induced release of endogenous opioids in individuals with gambling disorder (Mick, Myers et al. 2016).

Dopamine Systems

There is mixed evidence regarding the potential role for dopamine in gambling disorder (Potenza 2013, Potenza 2018). For example, CSF studies of men with gambling disorder as compared to those without found decreased levels of dopamine and elevated levels of the dopamine metabolites 3,4-dihydroxyphenylacetic acid (DOPAC) and homovannilic acid (HVA) in subjects with gambling disorder as compared to control subjects without the disorder (Bergh, Eklund et al. 1997). The authors of the study concluded that these findings were consistent with an increased rate of dopamine neurotransmission (Bergh, Eklund et al. 1997). However, when correcting for differential rates of CSF flow, these findings were no longer statistically significant (Nordin and Eklundh 1999), raising questions regarding the interpretation of the results.

The potential for dopamine involvement in gambling disorder remains poorly understood in other areas. Drug challenge studies have generated results that suggest a complicated role for dopamine and possibly other biogenic amine systems. In one study, amphetamine, a stimulant drug with pro-dopaminergic effects that also has substantial influences on other neurotransmitter systems including noradrenergic ones, was found to increase self-reported motivation to gamble in problem gamblers (Zack 2004). However, haloperidol, a drug that blocks D2/D3 receptors, was found to enhance the rewarding and priming effects of a gambling episode in disordered gamblers (Zack and Poulos 2007). This latter finding may in part explain why drugs that block dopamine neurotransmission have not been shown to be helpful in the treatment of gambling disorder in limited controlled trials that have been performed with such agents (Grant and Potenza 2007). The findings of both increases and decreases in dopamine D2/D3 receptor availability in people

with gambling disorder (Linnet, Peterson et al. 2010, Linnet, Moller et al. 2011) suggests a significant biological heterogeneity within the group of people with gambling disorder, and the findings of a relationship with mood-related impulsivity suggests that important individual differences in dopamine function might relate to specific behavioral tendencies that have been linked to gambling disorder (Clark, Stokes et al. 2012).

Glutamate Systems

Glutamate is a major excitatory neurotransmitter. Although it has been proposed to be involved in motivated behaviors like gambling for many years (Chambers and Potenza 2003), data supporting a potential role for glutamatergic drugs in the treatment of gambling disorder have only more recently been reported. For example, the neutraceutical and glutamate-modulating agent n-acetyl cysteine was found to be superior to placebo in a double-blind discontinuation study in gambling disorder (Grant, Kim et al. 2007). Openlabel treatment with another glutamatergic agent, memantine, was associated with improvement in problem gambling severity measures as well as with changes in cognitive function relating to compulsivity and impulsivity (Grant, Odlaug et al. 2010). A more recent randomized controlled trial found n-acetyl cysteine to help reduce tobacco consumption during treatment and problem-gambling severity after treatment in individuals with pathological gambling and nicotine dependence who received behavioral therapy targeting problematic gambling behaviors (Grant, Odlaug et al. 2014).

Neural Systems

Data suggest that specific brain regions are anatomically and functionally connected and work together as circuits during cognitive, emotional and motivational processes. Several brain regions that have been proposed to lie within a functional

neurocircuit have been implicated in impulse control disorders and addiction (Chambers and Potenza 2003, Chambers, Taylor et al. 2003). This circuitry is thought to involve cortico-striato-thalamo-cortical loops, and these loops serve as the basis for motivated drives and behaviors. This circuitry receives input from such regions as the hypothalamus, hippocampus, and amygdala that provide homeostatic, contextual memory, and affective information, respectively. Important to this circuitry that functions in part to make decisions based on risk-reward assessments are multiple frontal cortical regions, particularly the vmPFC.

The vmPFC has been implicated in a broad range of disorders and behaviors characterized by impaired impulse control. For example, associations between diminished activation of the vmPFC and imagined aggression have been observed (Pietrini, Guazzelli et al. 2000). Individuals with impulsive aggression have shown blunted activation of the vmPFC to the serotonergic drugs fenfluramine (Siever, Buchsbaum et al. 1999) and metachlorophenylpiperazine, or m-CPP (New, Hazlett et al. 2002). These findings extend studies of individuals with alcoholism in which similar findings (blunted responses to m-CPP, including within ventral cortex) were observed (Hommer, Andreasen et al. 1997). More recently, diminished activation of the vmPFC has been observed in individuals with gambling disorder during gambling urges (Potenza, Steinberg et al. 2003), cognitive control (Potenza, Leung et al. 2003), and simulated gambling (Reuter, Raedler et al. 2005).

Brain imaging studies of individuals with gambling disorder have identified differences in function in multiple other brain regions. Another brain region that is hypothesized to be important in motivated drives and behaviors, impulse control, and addiction is the ventral striatum or nucleus accumbens. This brain region has been

implicated in multiple functions including reward processing, reinforcement, and reward-based learning and memory (Volkow and Li 2004). Gambling disordered subjects as compared to control subjects have been found to show diminished activation of the ventral striatum during a simulated gambling task, and within the group of gambling disorder subjects, a strong inverse correlation between activation of this region and gambling disorder severity was observed (Reuter, Raedler et al. 2005). Additional studies (e.g., of reward processing (Balodis, Kober et al. 2012, Choi, Shin et al. 2012)) also indicate blunted activation of the ventral striatum during reward anticipation, as has been reported in alcohol dependence (Wrase, Schlagenhauf et al. 2007, Beck, Schlagenhauf et al. 2009), nicotine dependence (Peters, Bromberg et al. 2011) and other disorders characterized by impaired impulse control (Balodis, Kober et al. 2013, Balodis and Potenza 2015). Although the existing brain imaging studies should be considered preliminary in that they have small, selected samples, existing data suggest significant differences in brain function in individuals with and without pathological gambling.

Genetics

Substantial genetic influences have been found to contribute to psychiatric disorders including gambling disorder (Brewer and Potenza 2008). Much data have been derived from twin studies in which knowledge of zygosity (monozygotic or identical twins vs. dizygotic or fraternal twins) can be used to estimate genetic, unique environmental and shared environmental influences (Shah, Eisen et al. 2005). These data suggest that genetic contributions account for a significant component of the risk for gambling disorder and its co-occurrence with other psychiatric disorders including alcohol dependence (Slutske, Eisen et al. 2000), major depression (Potenza, Xian et al. 2005), anxiety disorders (Giddens

et al., 2011), drug-use disorders (Xian, Giddens et al. 2014), and obsessive-compulsive features (Scherrer, Xian et al. 2015). These studies have largely been performed in a sample of male twins whose characteristics might not be generalizable to all individuals with gambling disorder, although similar genetic contributions to gambling disorder appear to exist for both men and women (Slutske, Zhu et al. 2010). Overall, the findings suggest the importance in seeking to identify both specific genetic and environmental factors contributing to gambling disorder.

V. Individual Factors

Stressful Life Experiences

Stress has been associated with mental health conditions including gambling disorder. A study found that among 149 disordered gamblers, measures of childhood maltreatment were significantly and positively associated with earlier age at gambling onset and severity of gambling problems (Petry, Steinberg et al. 2005). In another study of 1675 male twins, child abuse, child neglect, witnessing someone badly hurt or killed, and physical attack were each associated with gambling disorder (Scherrer, Xian et al. 2007). Specific patterns of brain responses in individuals with and without gambling disorder may be linked to stress and functioning of adrenergic systems (Elman, Beccera et al. 2012). Other specific types of stress (e.g., that related to marital strain or poor physical health) may also relate importantly to gambling disorder (Southwell, Boreham et al. 2008, Voon, Sohr et al. 2011). Stress may also influence the relationships between problem-gambling severity and psychopathology (Ronzitti, Glenn et al. 2018). The relationship between stress, gambling and health measures more broadly may be important to consider given the associations between gambling problems and poor physical health.

VI. Psychiatric Co-Occurrences

It has been argued that gambling disorder, like other psychiatric disorders, is heterogeneous in nature and that this complicates the generation of an over-arching theory to explain the disorder (Blaszczynski and Nower 2002). Consistent with this notion and the idea of important individual differences is the observation that gambling disorder frequently co-occurs with other disorders (Crockford and el-Guebaly 1998, Petry, Stinson et al. 2005). Frequent co-occurrence of psychiatric disorders has been observed in both clinical and community-based samples. For example, in a large community-based population study, high rates of a wide range of DSM-IV Axis-I disorders (e.g. alcohol dependence, nicotine dependence, drug abuse, drug dependence, major depression, dysthymia, mania, panic disorder with agarophobia, panic disorder without agoraphobia, generalized anxiety disorder, social phobia, and specific phobia) and Axis-II disorders (avoidant, obsessive-compulsive, antisocial, schizoid, dependent, paranoid and histrionic) were observed in association with pathological gambling more so than in those without (Petry, Stinson et al. 2005).

Co-occurrences for Axis-I disorders seem particularly strong in women; for example, the relationships between problem/pathological gambling and major depression was stronger in women as compared to men, consistent with finding that women with pathological gambling tend more frequently to acknowledge gambling to escape from dysphoria (Blanco, Hasin et al. 2006, Desai and Potenza 2008). However, many disorders and psychiatric conditions (e.g., mania, alcohol abuse/dependence) were elevated in both women and men with subsyndromal/syndromal levels of gambling disorder (Desai and Potenza 2008). Importantly, some of these conditions may influence gambling behaviors.

For example, individuals with alcohol abuse/dependence often consume large quantities of alcohol, and alcohol consumption has been found to lead to more persistent gambling and larger losses on electronic gambling machines (Kyngdon and Dickerson 1999).

The nature of the co-occurrence between gambling disorder and psychiatric disorders remains incompletely understood. For example, consider individuals with major depression. People who are feeling depressed may gamble more to escape from the feeling of dysphoria (see inclusionary criterion #5), people with gambling disorder may become depressed (e.g., following significant financial losses or disruptions in major areas of life functioning (e.g., marital strain) related to the gambling), or a common etiology may contribute to both. Data supporting each of these possibilities can be found. For example, studies indicating that the vast majority of the overlap between gambling disorder and major depression is determined by shared genetic factors points toward the existence of a common etiology (Potenza, Xian et al. 2005). Similar studies indicating shared genetic and environmental contributions to gambling disorder and alcohol dependence similarly suggest that the complex contributions to the risk for developing gambling disorder include important heritable factors related to psychiatric disorders (Slutske, Eisen et al. 2000, Slutske, Eisen et al. 2001, Shah, Eisen et al. 2005), with molecular genetic risk alleles previously linked to risk for alcohol-use problems found to be associated with gambling disorder (Lang, Leménager et al. 2016). As such, individuals with family histories of not only gambling disorder, but also other genetically related disorders (alcohol dependence, antisocial behaviors, major depression, anxiety disorders) may be at increased risk for developing gambling disorder.

The findings of elevated levels of impulsivity in individuals with gambling disorder are consistent with my research findings and that of other groups as well as with my clinical experiences in having treated hundreds of people with gambling problems, some of which is found in published work (Grant 2003, Grant and Potenza 2004, Grant and Potenza 2006, Grant and Potenza 2006, Grant, Potenza et al. 2006), whereas much is not published (from non-research clinical practice). Given the importance of self-control and individual decision-making in gambling disorder, interventions that target self-control over desires to gamble or making decisions to engage in non-gambling behaviors (going to Gamblers Anonymous (GA) meetings or contacting a GA sponsor when a desire to gamble arises) are often used in clinical practice. GA teaches individuals through a step-wise process to take individual responsibility for their actions and the consequences thereof. Like with other 12-step programs, blame is not placed on an external object or person, but rather responsibility for one's own actions is achieved through alternate decision-making, making amends to others for harmful behaviors one performed related to excessive gambling, and helping others with similar life experiences. This pattern of taking individual responsibility for one's behaviors seems particularly helpful and empowering for individuals who are seeking to exhibit more self-control over areas of life. Although more research is needed to evaluate the specific mechanisms by which treatments for gambling disorder work (Walker 2006), behavioral approaches that incorporate techniques like those mentioned above have received empirical support in controlled studies (Petry 2003, Petry 2005, Petry 2005, Petry, Alessi et al. 2006).

Suicidality

Complexities exist in understanding the relationships between suicidality and recreational, problem and gambling disorder. One complexity arises from how best to define suicidality including suicidal thoughts (e.g., active and passive suicidal ideation) and suicidal behaviors (including various stages of planning attempts). Additionally, ascribing suicidality to any one factor may also be complicated, as described below.

Studies have suggested that individuals with gambling disorder may have elevated rates of suicidality. For example, while studies of the general population indicate that lifetime prevalence rates of suicidal ideation tend to range from 5% to 18%, suicidal plans from about 3% and actual attempts from about 1% to 5%, estimates in individuals in mental-health-care settings with gambling disorder or attendants of Gambler's Anonymous tend to report higher frequencies of suicidal ideation (17% to 80%) and suicide attempts (4% to 23%) (Maccallum and Blaszczynski 2003). We have also observed high rates of suicidality in people in treatment for gambling disorder, with 46% of patients reporting current suicidal ideation, and this was linked to problem-gambling severity, anxiety and depression (Ronzitti, Soldini et al. 2017). As suggested by this study, it is difficult to discern what might be related to gambling disorder and what might be better accounted for by other factors like other psychiatric disorders, particularly as individuals in these settings often have co-occurring disorders that might be related to suicidality.

Implications for Prevention and Treatment

The observation that gambling disorder co-occurs with a broad range of disorders carries significant implications for prevention and treatment. For example, there are data that individuals with co-occurring bipolar (Hollander, Pallanti et al. 2005), anxiety (Grant and Potenza 2006), psychotic (Chambers and Potenza 2001) or substance-use (Crockford

1998) disorders might respond preferentially el-Guebaly specific and pharmacotherapies, and treatment algorithms based on the presence or absence of cooccurring disorders have been proposed (Bullock and Potenza 2012, Yip and Potenza However, these algorithms should be considered preliminary given that 2014). comprehensive studies for effective treatments for gambling disorder are at an early stage and existing studies often have multiple limitations (Bullock and Potenza 2012, Yip and Potenza 2014). For reasons such as these, no drugs have been approved by the United States Food and Drug Administration to date with an indication for the treatment of gambling disorder. Although multiple behavioral therapies (e.g., cognitive behavioral therapy) have empirical support in the treatment of gambling disorder (Bullock and Potenza 2012, Yip and Potenza 2014), many individuals with gambling disorder go untreated (Slutske 2006).

VII. Conclusions

Gambling disorder shares many of the core features of addictions, including (i) continued engagement in behavior despite adverse consequences; (ii) diminished self-control; and (iii) an appetitive urge or craving state prior to the engagement in the behavior (Potenza 2006). These disorders have inclusionary criteria targeting tolerance, withdrawal, interference in major aspects of life functioning, and repeated unsuccessful attempts to cut back or quit (American Psychiatric Association, 2000; Potenza, 2006). Some criteria for gambling disorder appear more specific to gambling rathr than addiction more broadly. For example, the criteria targeting "chasing" (return to a gambling venue in an attempt to win back money recently lost) or "bail outs" (borrowing money to escape from a desperate financial situation related to gambling losses) seem more specific to gambling disorder,

although similar behaviors related to drug use are often exhibited by drug-dependent individuals (Potenza, 2006). As such, gambling disorder has been conceptualized as an "addiction without the drug" (Holden, 2001; Petry, 2006; Potenza, 2006). The disorder frequently goes unrecognized for considerable periods and can constitute a great threat to personal health and lead to criminal conduct in some cases.

VIII. Clinical Evaluation

In the following paragraphs, I will present findings from my evaluation of Mr. Michael Scronic. He was interviewed on May 23 of 2018. The clinical interview lasted between two-and-one-half and three hours and employed interviewing techniques that I typically use during the performance of clinical assessments in my clinical practice. Mr. Scronic was asked to complete several self-report instruments including the South Oaks Gambling Screen (SOGS), the Barratt Impulsiveness Scale (BIS-11) and the Toronto Alexithymia Scale (TAS-20). The first is a widely used gambling screen that assesses lifetime gambling-related attitudes and behaviors. The second is a widely used measure that assesses attentional, motor and non-planning aspects of impulsivity. The third is used to assess alexithymia, or difficulty in identifying and interpreting emotions. The following report is based upon the clinical interview and focuses on his gambling behaviors.

Demographics: Mr. Scronic reports being a 46-year-old married Caucasian male who lives in New York, NY (Manhattan) and reports going thorough a divorce with his wife Ashley. He and his wife have one son (MJ, 6 years of age). He reports currently working as a math tutor. He reports now engaging in meditation and trying to focus on his health.

Chief Complaint: "I have a gambling addiction."

History of Present Illness: Mr. Scronic reports a long history of gambling and gambling problems. He reports gambling in his college (for example, going on ski trips to Tahoe when he was at Stanford as an undergraduate) and going gambling about once or twice a month to gamble on blackjack. He reports continuing gambling in Atlantic City in the northeast and on lake or river locations while in the midwest while he was at the University of Chicago Business School. He reports at times staying longer than his friends at casinos. He reports at time having "maxed his ATM" when gambling. He reports at times having lost \$10,000 to \$15,000 during a trip to a casino. He reports that while on vacations he would also at times gamble at casinos. He also reports not thinking that he had a gambling problem as he thought he could afford the losses (for example, when he was working on Wall Street). He reports having felt similarly during trading as he did during gambling. He reports having felt like the trading took the place of blackjack gambling. Trading meets the definition of gambling (namely, placing something of value at risk in the hopes of gaining something of greater value).

In the early to mid 2000s, he reports having worked at Morgan Stanley. He reports having been promoted but then losing several millions of dollars due to risky trades. In this setting, he became depressed, anxious and briefly suicidal (passive, without attempt) leading to an evaluation in the emergency department at St Vincent's and subsequent outpatient treatment for approximately 6 months during which time he took venlafaxine and clonazepam. At the time, he reported sleep disturbances, difficulty concentrating, fatigue, anxiety with nausea that would come and go and not have onsets in sudden bursts,

anhedonia and passive suicidal ideation around the time of hospitalization. He reports having stopped the medication and going into trading as an independent entity or agent. He reports during the course of his independent trading having liquidated assets (e.g., sold an apartment in New York and started renting a house) in order to support his trading. He reports having taken funds from his wife's account woithout her knowledge to support his trading. He reports subsequently receiving funds from friends and family to invest to support his trading and received a large loan from a friend to support his trading. He reports having made false documents to indicate that investors were earning money rather than losing money in order for him to continue his trading.

He reports that with trading he made riskier trades of higher values over time, became irritable when he could not trade (when on vacation in Costa Rica), would think about trading to the extent that it interfered with sleep, engaged in illegal activities to support his trading, lied about how much money he lost or made while trading. He reports the trading and the lies surrounding the trading led to interference in major areas of life functioning (e.g., with his wife separating from and in the process of divorcing him, and him having lost or left a job at Morgan Stanley from losing money in the setting of making risky trades). He reports while trading having experienced some racing thoughts and a decreased need for sleep that were relatively stable over time and accompanied by high level caffeine consumption during the day (perhaps 8-10 cups of coffee per day) and heavy alcohol consumption in the evening.

He reports that in October 2017, the FBI charged him with security fraud and that he was hospitalized at New York Presbytarian. The inpatient admission was for stabilization and for concerns that he might harm himself given the recent arrest and the possible implications with respect to serving time in jail and the impact on his family. During the hospitalization, concerns were raised regarding depression and anxiety. However, a diagnosis of a personality disorder (narcissitic with antisocial features) was noted later in the course of the hospitalization given that there was not sufficient evidence for an active disorder of depression, bipolar disorder, anxiety disorder or psychotic disorder. It was also noted that he did not seem to fully appreciate the impact that his trading behaviors and the misrepresentation of the use of funds trusted to him may have on relationships with them.

During his hospitalization, it was noted that he screened positive for hazardous or heavy drinking. During the interview, he reported heavy drinking during college (including at times 12 drinks per night with blackouts) and several drinking and driving incidents with one in 2015 leading to the need for him to take a course and one where he drove his jeep into a tree. He reported having concealed the extent of his alcohol use and reported recent craving for alcohol. He reported that he was planning to attend Alcoholics Anonymous (AA) the week of the interview and that he was discussing his alcohol use problem within the refuge recovery program (a recovery program employing mindfulness and Buddhist philosophies).

He reports having been attending Gamblers Anonymous weekly following his inpatient hospitalization. He reports having a sponsor in the program. He reports meeting with a

clinician (Mr. Hodel) to focus on recovery, and Mr, Hodel diagnosed him with a

generalized anxiety disorder and a gambling disorder. He denies feeling depressed

presently and reports focusing on health, having lost weight (from 220 pounds to 180),

meditating on a daily basis, and exercising regularly.

He denies auditory/visual hallucinations, manic symptoms, paranoia, recent use of illicit

substances (reports some cannabis in college), or active anxiety or depression.

Medications: Reports not taking any medications.

Allergies: Reports no known drug allergies.

Past medical history: Reports elevated BP but "not high enough to start medications".

Reports recent skin cancer removal. Reports prior obesity with being overweight presently.

Past psychiatric history: Reports having been seen at a walk-in emergency clinic in 2005

at St. Vincents Hospital for major depression with suicidality, with rule outs for generalized

anxiety disorder and bipolar disorder. Reports having been hospitalized at NY Presbyterian

Hospital in October 2017 as described above. Reports being in treatment with Mr. Hodel

and attenting 12-step programs for gambling and alcohol-use problems.

Family history: Reports maternal aunt who had a lobotomy (diagnosis not known). Reports

paternal grandfather who was an abusive alcoholic. Mother reportedly rapidly lost her ex-

husband's retirement money in the stock market. Mother allegedly reported abuse in the

25

divorce process. Mr. Scronic was unclear regarding the specifics and wished not to discuss

further. Maternal grandfather reportedly "lost all the family money at the track."

Social: Reports having been raised in a supportive environment; denies school problems

during K-12 schooling (reports having skipped a grade and having done well

academcially); denies physical or sexual abuse; reports graduating with an undergraduate

degree (double major) from Stanford University and a business school degree from

University of Chicago; denies military involvement; reports current legal concerns related

to FBI charges.

Mental Status: engaged in interview; slightly fidgety; casually dressed; neatly groomed;

speech: slightly rapid, slightly loud and slightly increased amount; sometimes interrupts

interviewer; mood: "good"; affect: mildly anxious; thought process: largely goal-directed

but mildly tangential and circumstantial; thought content: no suicidal or homicidal ideation

reported; no hallucinations; cognition: alert, oriented; names, repeats, follows commands;

WORLD-DLROW; 3/3 at 0 min, 3/3 at 5 min; serial 7's to 65; presidents: Trump->Obama-

>Bush->Clinton->Bush; NY-LA 3,000 miles; mail letter; runs out of theater for fire; copies

pentagons

Lifetime SOGS score: 17

Barratt Impulsiveness Scale: Total: 101; Attentional: 27; Motor: 34; Non-planning: 40

Toronto Alexithymia Scale: Total: 82; Defficulty Identifying Feelings: 29; Describing

Feelings: 24; Externally Oriented Thinking: 29

26

Assessment: Upon examination and with some collateral information (from records from St. Vincent's and New York Presbyterian and a letter from Mr. Hodel), Mr. Scronic meets criteria for a moderate to severe gambling disorder in reported early remission (what was termed pathological gambling in the DSM-IV), consistent with his SOGS score. His preferred forms of gambling involved blackjack and trades on the stock market. His BIS-11 score indicates a high level of impulsivity, a characteristic often found in conjunction with gambling disorder. He also exhibits a high level of alexithymia, another characteristic also associated with gambling disorder. He also appears to meet criteria for lifetime alcohol use disorder, generalized anxiety disorder and major depression. Personality characteristics noted in his hospitalization at New York Presbyterian also warrant consideration as multiple personality disorders (including narcisistic personality disorder) have been observed to co-occur with gambling disorder.

I believe that Mr. Scronic's psychiatric conditions should be given serious consideration in fashioning his sentencing. As an increasingly growing literature emerges on the neurobiological underpinnings of gambling disorder, there exists a firm foundation on which to base such consideration. I hope that this letter is helpful to the Court.

Sincerely,

Marc N. Potenza, M.D., Ph.D.

Senior Scientist, The Connecticut Council on Problem Gambling

Professor of Psychiatry, Child Study and Neuroscience

Yale University School of Medicine

References

Abbott, M. W., U. Romild and R. A. Volberg (2014). "Gambling and problem gambling in Sweden: changes between 1998 and 2009." J Gambl Stud **30**(4): 985-999.

Arnsten, A. F. (2001). "Modulation of prefrontal cortical-striatal circuits:

relevance to therapeutic treatments for Tourette syndrome and attention-deficit hyperactivity disorder." Adv Neurol 85: 333-341.

Arnsten, A. F. and B. M. Li (2005). "Neurobiology of executive functions: catecholamine influences on prefrontal cortical functions." Biological Psychiatry 57(11): 1377-1384. Association, A. P. (2000). Diagnostic and Statistical Manual of Mental

Disorders. Fourth Edition-Test Revision. Washington, DC, American

Psychiatric Association.

Association, A. P. (2013). <u>Diagnostic and Statistical Manual of Mental Disorders</u>. Fifth Edition. Washington, DC, American Psychiatric Association.

Balodis, I. M., H. Kober, P. D. Worhunsky, M. C. Stevens, G. D. Pearlson and M. N. Potenza (2012). "Diminished fronto-striatal activity during processing of monetary rewards and losses in pathological gambling." Biol

Psychiatry **71**: 749-757.

Balodis, I. M., H. Kober, P. D. Worhunsky, M. A. White, M. C. Stevens, G. D. Pearlson, R. Sinha, C. M. Grilo and M. N. Potenza (2013). "Monetary reward processing in obese individuals with and without binge eating disorder. ." <u>Biological Psychiatry</u> **73**: 877-886. Balodis, I. M. and M. N. Potenza (2015). "Anticipatory reward processing in

addicted populations: a focus on the monetary incentive delay task." Biol

Psychiatry 77: 434-444.

Beck, A., F. Schlagenhauf, T. Wustenberg, J. Hein, T. Kienast, T. Kahnt, K. Schmack, C. Hagele, B. Knutson, A. Heinz and J. Wrase (2009). "Ventral striatal activation during reward anticipation correlates with impulsivity in alcoholics." Biol Psychiatry 66: 734-742.

Bergh, C., T. Eklund, P. Sodersten and C. Nordin (1997). "Altered dopamine function in pathological gambling." <u>Psychological Medicine</u> **27**(2): 473-

Blanco, C., D. S. Hasin, N. Petry, F. S. Stinson and B. F. Grant (2006). "Sex differences in subclinical and DSM-IV pathological gambling: results from the National Epidemiologic Survey on Alcohol and Related Conditions." Psychological Med 36: 943-953.

Blaszczynski, A. and L. Nower (2002). "A pathways model of problem and pathological gambling." Addiction 97: 487-499.

Blumberg, H. P., H. Leung, P. Skudlarski, C. M. Lacadie, C. A. Fredericks, B. C. Harris, D. S. Charney, J. C. Gore, J. H. Krystal and B. S. Peterson (2003). "A functional magnetic resonance imaging study of bipolar

(2003). "A functional magnetic resonance imaging study of bipolar disorder: state- and trait-related dysfunction in ventral prefrontal cortices." Archives of General Psychiatry **60**: 599-607. Brewer, J. A. and M. N. Potenza (2008). "The Neurobiology and Genetics of

Impulse Control Disorders: Relationships to Drug Addictions." Biochem

Pharmacology 75: 63-75.

Bullock, S. A. and M. N. Potenza (2012). "Pathological gambling: Neuropsychopharmacology and treatment." <u>Curr Psychopharmacol</u> 1: 67-

Chambers, R. A. and M. N. Potenza (2001). "Schizophrenia and pathological gambling." Am J Psychiatry 158: 497-498.

Chambers, R. A. and M. N. Potenza (2003). "Neurodevelopment, impulsivity and adolescent gambling." <u>J Gambling Stud</u> **19**(1): 53-84. Chambers, R. A., J. R. Taylor and M. N. Potenza (2003). "Developmental

neurocircuitry of motivation in adolescence: A critical period of addiction vulnerability." Am J Psychiatry 160: 1041-1052.
Choi, J.-S., Y.-C. Shin, W. H. Jung, J. H. Jang, D.-H. Kang, C.-H. Choi, S.-W. Choi, J.-Y. Lee, J. Y. Hwang and J. S. Kwon (2012). "Altered Brain Activity during Reward Anticipation in Pathological Gambling and Obsessive-Compulsive Disorder." PLoS One 7(9): e45938.

Clark L. P. P. Stokes, K. Wu, P. Michaleguk, A. Benegke, R. L. Watson, A.

Clark, L., P. R. Stokes, K. Wu, R. Michalczuk, A. Benecke, B. J. Watson, A. Egerton, P. Piccini, D. J. Nutt, H. Bowden-Jones and A. R. Lingford-Hughes (2012). "Striatal dopamine D2/D3 receptor binding in pathological gambling is correlated with mood-related impulsivity." Neuroimage 63: 40-46.

Crockford, D. N. and N. el-Guebaly (1998). "Psychiatric comorbidity in pathological gambling: a critical review." <u>Canadian Journal of Psychiatry</u>

- Revue Canadienne de Psychiatrie 43(1): 43-50. DeCaria, C., Hollander, E (1993). Pathological gambling. Obsessivecompulsive related disorders. E. Hollander. Washington, DC, American

Psychiatric Press: 155-178.

- DeCaria, C. M., T. Begaz and E. Hollander (1998). "Serotonergic and noradrenergic function in pathological gambling." CNS Spectrums 3(6): 38-47.
- Desai, R. A. and M. N. Potenza (2008). "Gender differences in the associations between problem gambling and psychiatric disorders." <u>Soc Psychol Psychiatr Epi</u> **43**: 173-183.

Eber, G. B. and H. J. Shaffer (2000). "Trends in bio-behavioral gambling

studies research: Quantifying citations." <u>J Gambling Stud</u> **16**: 461-467.

Elman, I., L. Beccera, E. Tschibelu, R. Yamamoto, E. George and D. Borssok (2012). "Yohimbine-Induced Amygdala Activation in Pathological Gamblers: A Pilot Study." <u>PLoS One</u> **7**(2): e31118.

Grant, J., Kim SW, Potenza MN, Blanco C, Ibanez A, Stevens LC, Zaninelli R (2003). "Parovetine treatment of pathological gambling: A multi-center

R (2003). "Paroxetine treatment of pathological gambling: A multi-center randomized controlled trial." Int Clin Psychopharmacol 18: 243-249.

- Grant, J. and M. N. Potenza (2004). "Impulse control disorders: clinical characteristics and pharmacological management." Ann Clin Psychiatry **16**: 27-34.
- Grant, J. and M. N. Potenza (2006). Impulse Control Disorders A Clinical Text of Men's Mental Health. J. E. Grant and M. N. Potenza. Washington, DC.
- Grant, J. E., S. W. Kim and B. K. Hartman (2008). "A double-blind, placebocontrolled study of the opiate antagonist naltrexone in the treatment of pathological gambling urges." <u>J Clin Psychiatry</u> **69**: 783-789. Grant, J. E., S. W. Kim, E. Hollander and M. N. Potenza (2008). "Predicting

Response to Opiate Antagonists and Placebo in the Treatment of

Pathological Gambling." <u>Psychopharmacol</u> **200**: 521-527. Grant, J. E., S. W. Kim and B. L. Odlaug (2007). "N-Acetyl cysteine, a glutamate-modulating agent, in the treatment of pathological gambling: a pilot study." Biol Psychiatry 62: 652-657.

Grant, J. E., B. L. Odlaug, S. R. Chamberlain, M. N. Potenza and S. W. Kim (2010). "Open-Label Memantine Treatment of Pathological Gambling

Cognitive Reduces Gambling Severity Inflexibility." and

Psychopharmacology 4: 603-612.

Grant, J. E., B. L. Odlaug, S. R. Chamberlain, M. N. Potenza, L. R. Schreiber, C. B. Donahue and S. W. Kim (2014). "A randomized, placebo-controlled trial of N-acetylcysteine plus imaginal desensitization for nicotine-dependent pathological gamblers." J Clin Psychiatry 75(1): 39-45.

Grant, J. E., B. L. Odlaug, M. N. Potenza, E. Hollander and S. W. Kim (2010). "A Multi-Center, Double-Blind, Placebo-Controlled Study of the Opioid Antagonist Nalmefene in the Treatment of Pathological Gambling." Brit J

Psychiatry 197: 330-331.

- Grant, J. E. and M. N. Potenza (2006). "Escitalopram Treatment of Pathological Gambling with Co-Occurring Anxiety: An Open-Label Pilot Study with Double-Blind Discontinuation." Int Clin Psychopharmacol 21: 203-209.
- Grant, J. E. and M. N. Potenza (2007). Treatments for pathological gambling and other impulse control disorders. A Guide to Treatments That Work. G.
- J. Nathan P. Oxford, UK, Oxford University Press: 561-577.
 Grant, J. E., M. N. Potenza, E. Hollander, R. M. Cunningham-Williams, T. Numinen, G. Smits and A. Kallio (2006). "Multicenter investigation of the opioid antagonist nalmefene in the treatment of pathological gambling. Am J Psychiatry **163**: 303-312.

Hoffmann, J., Gerstein, D, Larison, C, Huang, L, Brittingham, A, Toce, M. (1999). "Report to the National Gambling Impact Study Commission."

Retrieved April 14, 1999.

Hollander, E., Begaz, T, DeCaria, C (1998). "Pharmacologic approaches in the treatment of pathological gambling." CNS Spectrums 3(6): 72-80.

Hollander, E., S. Pallanti, A. Allen, E. Sood and N. B. Rossi (2005). "Does Systemed Belosse Lithium Badras Impulsive Cambling and Affective Complete."

Sustained-Release Lithium Reduce Impulsive Gambling and Affective Instability Versus Placebo in Pathological Gamblers With Bipolar Spectrum Disorders?" Am J Psychiatry 162: 137-145.

Hollander, E., Wong CM (1995). "Obsessive-compulsive spectrum disorders." J Clin Psychiatry 56s4: 3-6.

Hommer, D., P. Andreasen, D. Rio, W. Williams, U. Rettimann, R. Monenan,

A. Zametkin, R. Rawlings and M. Linnoila (1997). "Effects of mchlorophenylpiperazine on regional brain glucose utilization: A positron emission tomographic comparison of alcoholic and control subjects." J Neurosci 17: 2796-2806.

Institute for Research on Pathological Gambling and Related Disorders (2006). "Toward Evidence-Based Responsible Gaming Policies and Practices: New Grants for Translational research on Gambling and Gambling Disorders."

http://www.divisiononaddictions.org/institute/rfa/translationalrfa.pdf

Accessed: March 15, 2006.

- Kessler, R. C., I. Hwang, R. LaBrie, M. Petukhova, N. A. Sampson, K. C. Winters and H. J. Shaffer (2008). "DSM-IV pathological gambling in the National Comorbidity Survey Replication." <u>Psychological Med</u> **38**: 1351-
- Kim, S. W., J. E. Grant, D. E. Adson and Y. C. Shin (2001). "Double-blind naltrexone and placebo comparison study in the treatment of pathological gambling." <u>Biol Psychiatry</u> **49**: 914-921.

Kyngdon, A. and M. Dickerson (1999). "An experimental study of the effect of prior alcohol consumption on a simulated gambling activity." Addiction

94: 697-707.

Lang, M., T. Leménager, F. Streit, M. Fauth-Bühler, J. Frank, D. Juraeva, S. Lang, M., T. Lemenager, F. Streit, M. Fauth-Bühler, J. Frank, D. Juraeva, S. H. Witt, F. Degenhardt, A. Hofmann, S. Heilmann-Heimbach, F. Kiefer, B. Brors, H. J. Grabe, U. John, A. Bischof, G. Bischof, U. Völker, G. Homuth, M. Beutel, P. A. Lind, S. E. Medland, W. S. Slutske, N. G. Martin, H. Völzke, M. M. Nöthen, C. Meyer, H. J. Rumpf, F. M. Wurst, M. Rietschel and K. F. Mann (2016). "Genome-wide association study of pathological gambling." Eur Psychiatry 36: 38-46.

Leeman, R. F. and M. N. Potenza (2012). "Similarities and Differences between Pathological Gambling and Substance Use Disorders: A Focus on Impulsivity and Compulsivity." Psychopharmacol 219: 469-490.

Linnet, J., A. Moller, E. Peterson, A. Gjedde and D. Doudet (2011). "Inverse association between donaminergic neurotransmission and Iowa Gambling."

association between dopaminergic neurotransmission and Iowa Gambling Task performance in pathological gamblers and healthy controls." Scand J Psychology **52**: 28-34.

Linnet, J., E. Peterson, D. J. Doudet, A. Gjedde and A. Moller (2010). "Dopamine release in ventral striatum of pathological gamblers losing money." Acta Psychiatrica Scand 122: 326-333.

Maccallum, F. and A. Blaszczynski (2003). "Pathological gambling and suicidality: an analysis of severity and lethality." Suicide Life Threat Behay 33: 88-98.

Meyer, G., J. Schwertfeger, M. S. Exton, O. E. Janssen, W. Knapp, M. A. Stadler, M. Schedlowski and T. H. Kruger (2004). "Neuroendocrine response to casino gambling Psychoneuroendocrinology **29**: 1272-1280. īn gamblers." problem

Mick, I., J. Myers, A. C. Ramos, P. R. Stokes, D. Erritzoe, A. Colasanti, R. N. Gunn, E. A. Rabiner, G. E. Searle, A. D. Waldman, M. C. Parkin, A. D. Brailsford, J. C. Galduróz, H. Bowden-Jones, L. Clark, D. J. Nutt and A. R. Lingford-Hughes (2016). "Blunted Endogenous Opioid Release Following an Oral Amphetamine Challenge in Pathological Gamblers.' New, A. S., E. A. Hazlett, M. S. Buchsbaum, M. Goodman, D. Reynolds, V.

Mitropoulou, L. Sprung, J. R. B. Shaw, H. Konigsberg, J. Platholi, J. Silverman and L. J. Siever (2002). "Blunted prefrontal cortical 18fluorodeoxyglucose positron emission tomography response to meta-chlorophenylpiperazine in impulsive aggression." Arch Gen Psychiatry

59: 621-629.

Nordin, C. and T. Eklundh (1999). "Altered CSF 5-HIAA disposition in pathologic male gamblers." CNS Spectrums 4(12): 25-33.

Peters, J., U. Bromberg, S. Schneider, S. Brassen, M. Menz, T. Banaschewski, P. J. Conrod, H. Flor, J. Gallinat, H. Garavan, A. Heinz, B. Itterman, M. Lathrop, J. L. Martinot, T. Paus, J. B. Poline, T. W. Robbins, M. Rietschel, M. Smolka, A. Ströhle, M. Struve, E. Loth, G. Schumann, C. Büchel and I. Consortium. (2011). "Lower ventral striatal activation during reward anticipation in adelegacent amelers." Am J. Pavehintry 169: 540-540. anticipation in adolescent smokers." <u>Am J Psychiatry</u> **168**: 540-549. Petry, N. M. (2003). "Patterns and correlates of gamblers anonymous

attendance in pathological gamblers seeking professional treatment."

<u>Addictive Behaviors</u> **28**: 1049-1062.

Petry, N. M. (2005). "Gamblers Anonymous and Cognitive-Behavioral Therapies for Pathological Gamblers." J Gambling Stud **21**: 27-33.

Petry, N. M. (2005). Pathological gambling: Etiology, comorbidity and treatment. Washington, DC, American Psychological Association.

Petry, N. M. (2006). "Should the scope of addictive behaviors be broadened to include pathological gambling? ." <u>Addiction</u> **101**(s1): 152-160.

Petry, N. M., S. M. Alessi, K. M. Carroll, T. Hanson, S. MacKinnon, B. Rounsaville and S. Sierra (2006). "Cognitive-Behavioral Therapy for Pathological Gamblers." J Consult Clin Psychology 74: 555-567.

Petry, N. M., C. Blanco, M. Auriacombe, G. Borges, K. Bucholz, T. J. Crowley, B. F. Grant, D. S. Hasin and C. O'Brien (2014). "An overview of and rationale for changes proposed for pathological gambling in DSM-5." I Gamble Stud 30(2): 403-502 J Gambl Stud 30(2): 493-502.

Petry, N. M., C. Blanco, R. Stinchfield and R. Volberg (2013). "An empirical evaluation of proposed changes for gambling diagnosis in the DSM-5." Addiction 108(3): 575-581.

Petry, N. M., K. L. Steinberg and Women's Problem Gambling Research Center (2005). "Childhood maltreatment in male and female treatment-seeking pathological gamblers." Psychology Addict Behav 19: 226-229. Petry, N. M., F. S. Stinson and B. F. Grant (2005). "Co-morbidity of DSM-IV

- pathological gambling and other psychiatric disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions." <u>J</u> <u>Clin Psychiatry</u> **66**: 564-574.
- Pietrini, P., M. Guazzelli, G. Basso, K. Jaffe and J. Grafman (2000). "Neural correlates of imaginal agressive behavior assessed by positron emission tomography in healthy subjects." Am J Psychiatry 157: 1772-1781.

 Potenza, M. N. (2006). "Should addictive disorders include non-substance-related conditions?" Addiction 101(s1): 142-151.

 Potenza, M. N. (2008). "The neurobiology of pathological gambling and drug addiction: an overview and new findings." Phil Trans. P. See P. 363:

- addiction: an overview and new findings." Phil. Trans. R. Soc. B 363: 3181-3189.
- Potenza, M. N. (2013). "How central is dopamine to pathological gambling or gambling disorder?" Front Behav Neurosci 7: 206. Potenza, M. N. (2018). "Searching for Replicable Dopamine-Related Findings

in Gambling Disorder." Biol Psychiatry 83(12): 984-986.

Potenza, M. N. and E. Hollander (2002). Pathological Gambling and Impulse Control Disorders. Neuropsychopharmacology: The 5th Generation of Progress. J. C. C Nemeroff, D Charney, K Davis. Baltimore, MD, Lippincott Williams and Wilkens: 1725-1742.

Potenza, M. N., L. M. Koran and S. Pallanti (2009). "The relationship between impulse control disorders and obsessive—compulsive disorder: A current understanding and future research directions." Psychiatry Res 170: 22-31.

Potenza, M. N., T. R. Kosten and B. J. Rounsaville (2001). "Pathological gambling." JAMA 286: 141-144.
Potenza, M. N., H. C. Leung, H. P. Blumberg, B. S. Peterson, P. Skudlarski,

- C. Lacadie and J. C. Gore (2003). "An fMRI stroop study of ventromedial prefrontal cortical function in pathological gamblers." Am J Psychiatry **160**: 1990-1994.
- Potenza, M. N., M. A. Steinberg, P. Skudlarski, R. K. Fulbright, C. M. Lacadie, M. K. Wilber, B. J. Rounsaville, J. C. Gore and B. E. Wexler (2003). "Gambling urges in pathological gamblers: An fMRI study." Arch Gen Psychiatry 60: 828-836.

Potenza, M. N., H. Xian, K. Shah, J. F. Scherrer and S. A. Eisen (2005). "Shared genetic contributions to pathological gambling and major depression in men." Arch Gen Psychiatry 62: 1015-1021.
Reuter, J., T. Raedler, M. Rose, I. Hand, J. Glascher and C. Buchel (2005).

"Pathological gambling is linked to reduced activation of the mesolimbic reward system." Nature Neuroscience 8: 147-148.

Ronzitti, S., C. E. Glenn, S. W. Kraus, R. A. Hoff and M. N. Potenza (2018). "Stress Moderates the Relationships Between Problem-Gambling Severity and Specific Psychopathologies." <u>Psychiatry Res.</u> **59:**254-261. Ronzitti, S., E. Soldini, N. Smith, M. N. Potenza, M. Clerici and H. Bowden-

Jones (2017). "Lifetime and current suicidal ideation in treatment-seeking individuals in the United Kingdom with gambling problems." Addict Behav 74: 33-40.

Roy, A., B. Adinoff, L. Roehrich, D. Lamparski, R. Custer, V. Lorenz, M. Barbaccia, A. Guidotti, E. Costa and M. Linnoila (1988). "Pathological gambling. A psychobiological study." <u>Archives of General Psychiatry</u>

45(4): 369-373.

Roy, A., J. de Jong and M. Linnoila (1989). "Extraversion in pathological gamblers: Correlates with indexes of noradrenergic function." Archives of

General Psychiatry **46**(8): 679-681.

Scherrer, J. F., H. Xian, J. M. K. Kapp, B. Waterman, Shah, K R, , R. Volberg and S. A. Eisen (2007). "Association Between Exposure to Childhood and Lifetime Traumatic Events and Lifetime Pathological Gambling in a Twin Cohort." J Nerv Mental Dis 195: 72-78.

Scherrer, J. F., H. Xian, W. S. Slutske, R. Volberg, K. R. Shah, S. E. Eisen and M. N. Potenza (2015). "Associations Between Obsessive-Compulsive Classes and Pathological Gambling in a National Cohort of Male Twins.'

JAMA Psychiatry 72(4): 342-349.

Shah, K. R., S. A. Eisen, H. Xian and M. N. Potenza (2005). "Genetic studies of pathological gambling: A review of methodology and analyses of data from the Vietnam Era Twin (VET) Registry." J Gambling Stud 21: 177-

Siever, L. J., M. S. Buchsbaum, A. S. New, J. Spiegel-Cohen, T. Wei, E. A. Hazlett, E. Sevin, M. Nunn and V. Mitropoulou (1999). "d,l-fenfluaramine personality disorder impulsive assessed [18F]fluorodexyglucose positron emission tomography." Neuropsychopharmacology **20**: 413-423. Slutske, W. S. (2006). "Natural recovery and treatment-seeking in

pathological gambling: results of two national surveys." Am J Psychiatry

163: 297-302.

Slutske, W. S., S. Eisen, W. R. True, M. J. Lyons, J. Goldberg and M. Tsuang (2000). "Common genetic vulnerability for pathological gambling and

alcohol dependence in men." Arch Gen Psychiatry 57: 666-674.

Slutske, W. S., S. Eisen, H. Xian, W. R. True, M. J. Lyons, J. Goldberg and M. Tsuang (2001). "A twin study of the association between pathological gambling and antisocial personality disorder." J Abnorm Psychology 110: 297-308.

Slutske, W. S., G. Zhu, M. H. Meier and N. G. Martin (2010). "Genetic and Environmental Influences on Disordered Gambling in Men and Women."

Arch Gen Psychiatry(67): 624-630.

Southwell, J., P. Boreham and W. Laffan (2008). "Problem gambling and the circumstances facing older people: a study of gaming machine players aged 60+ in licensed clubs." J Gambl Stud 24(2): 151-174.

Volkow, N. D. and T.-K. Li (2004). "Drug addiction: The neurobiology of behavior gone awry." Nat Rev Neurosci 5: 963-970.

Voon, V., M. Sohr, A. E. Lang, M. N. Potenza, A. D. Siderowf, J. Whetteckey, D. Weintreck, C. P. Weintreck, C. P

D. Weintraub, G. R. Wunderlich and M. A. Stacy (2011). "Impulse control disorders in Parkinson disease: a multicenter case-control study." Ann Neurology **69**: 986-996.

Walker, M., Toneatto T, Potenza MN, Petry N, Ladouceur R, Hodgins DC, el-Guebaly N, Echeburua E, Blaszczynski A (All authors contributed equally to the generation of the manuscript) (2006). "A Framework for Reporting Outcomes in Problem Gambling Treatment Research: The Banff, Alberta Consensus." Addiction 101: 504-511.

Welte, J. W., G. M. Barnes, M. C. Tidwell, J. H. Hoffman and W. F. Wieczorek (2015). "Gambling and Problem Gambling in the United States: Changes Between 1999 and 2013." I Gambl Stud 31(3): 605-715.

Changes Between 1999 and 2013." J Gambl Stud 31(3): 695-715.
Welte, J. W., M. C. Tidwell, G. M. Barnes, J. H. Hoffman and W. F. Wieczorek (2016). "The Relationship Between the Number of Types of Legal Gambling and the Rates of Gambling Behaviors and Problems

Across U.S. States." J Gambl Stud 32(2): 379-390.

Wrase, J., F. Schlagenhauf, T. Kienast, T. Wustenberg, F. Bermpohl, T. Kahnt, A. Beck, A. Strohle, G. Juckel, B. Knutson and A. Heinz (2007).

"Dysfunction of reward processing correlates with alcohol craving in detoxified alcoholics." Neuroimage 35(2): 787-794.

Xian, H., J. Giddens, J. Scherrer, S. A. Eisen and M. N. Potenza (2014). "Environmental Factors Selectively Impact Co-occurrence of Problem/Pathological Gambling with Specific Drug-Use Disorders." Addiction 109: 635-644.

Yip, S. W. and M. N. Potenza (2014). "Treatment of Gambling Disorders."

Current Treatment Options in Psychiatry 1(2): 189-203.

Zack, M., Poulos CX (2004). "Amphetamine primes motivation to gamble and gambling-related semantic networks in problem gamblers." Neuropsyhcopharmacology **29**: 195-207. Zack, M. and C. X. Poulos (2007). "A D2 antagonist enhances the rewarding

and priming effects of a gambling episode in pathological gamblers. Neuropsychopharmacol **32**: 1678-1686.